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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/384,248	02/06/1995	MARC ALIZON	3495.0008-08	9162

22852 7590 03/10/2006

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EXAMINER	
PARKIN, JEFFREY S	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 03/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/384,248	ALIZON ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Office Action

Status of the Claims

Claims 34-36 are pending in the instant application. In response to the Decision On Appeal dated 12 July, 2005, applicants filed an amendment. Purportedly the board raised a new ground of rejection under 35 U.S.C. § 101 but affirmed the examiner's rejection of the claims under the written description requirement of 35 U.S.C. § 112, first paragraph. Applicants' amendment to the claim language obviates whatever grounds of rejection may have been raised by the Board.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

Claims 34-36 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). The claimed invention is directed toward methods for the production of antibodies to HIV-1 antigens encoded by three λ-J19 restriction fragments (e.g., *Kpn*I (~6,100)/*Bgl*II (~9,150); *Kpn*I (~3,500)/*Bgl*II

(~6,500); and, *Pst*I (~800)/*Kpn*I (3,500)). Presumably these restriction fragments correspond to the *gag*, *pol*, and *env* genes. The disclosure does **not** provide the complete nucleotide sequences of any of these restriction fragments, evidence that *bona fide* viral antigens were produced from said fragments, evidence that recombinant antigens were expressed and purified, and evidence that said recombinant antigens were administered to a suitable host to generate antibodies, and that said resultant antibodies were isolated and purified.

The written description requirement under Section 112, first paragraph, stipulates that the claimed subject matter must be supported by an adequate written description that is sufficient to enable anyone skilled in the art to make and use the invention. The courts have decided that the specification must demonstrate that the inventor had possession of the claimed invention as of the filing date relied upon. Although the claimed subject matter need not be described identically, nonetheless, the disclosure relied upon must convey to those skilled in the art that applicants had invented the subject matter claimed. *Ralston Purina Company* v. *Far-Mar-Co., Inc.*, 227 U.S.P.Q. 177 (C.A.F.C. 1985). *In re Wilder, et al.*, 222 U.S.P.Q. 369 (C.A.F.C. 1984). *In re Wertheim, et al.*, 191 U.S.P.Q. 90 (C.C.P.A. 1976). *In re Blaser, Germscheid,* and *Worms*, 194 U.S.P.Q. 122 (C.C.P.A. 1977). *In re Driscoll*, 195 U.S.P.Q. 434 (C.C.P.A. 1977). *Utter* v. *Hiraga*, 6 U.S.P.Q.2d 1709 (C.A.F.C. 1988).

This rejection is not based upon enablement considerations. The Examiner does not dispute the scientific findings that the skilled artisan, at the time of filing, provided with a restriction fragment capable of encoding a **known** antigen, could express and purify the antigen of interest and employ this protein to generate antigen-specific antibodies. **This rejection is based upon the inability of the disclosure to reasonably convey to the skilled**

artisan that applicants were in possession of the claimed HIV-1 antigens and antibodies at the time of the filing date relied upon. The specification fails to provide any demonstrative evidence that applicants had generated expression vectors containing the claimed inserts, transfected suitable hosts, and produced suitable levels of recombinant HIV-1 proteins. Moreover, **the disclosure fails to provide any evidence suggesting that these antigens were used to immunize animals and that HIV-1-specific antibodies were actually generated.**

The disclosure describes the preparation of a cDNA library from a LAV-infected immortalized B-lymphocyte cell line (see pp. 5 and 6). The cDNA library was screened and three recombinant clones (pLAV 13, pLAV 75, and pLAV 82) carrying LAV inserts identified (see p. 7). Having obtained short fragments of the LAV genome which should prove useful as probes, a second partial *Hind* III digested library was created from LAV-infected cells and screened for LAV proviral clones (p. 9). A series of positive clones were identified (lambda-J61, -J27, -J31, -J19) and their restriction maps ascertained (see pp. 2-4). Complete nucleotide sequences for these various clones were **not** provided. Considering the infidelity associated with the reverse transcription reaction in the preparation of cDNA libraries, and the quasispecies nature of retroviral infection which leads to many defective species, it is not readily manifest that any of these fragments encode proteins. The disclosure does **not** describe the insertion of these fragments into suitable expression vectors to see if they are capable of producing an immunogen. The disclosure does **not** describe the isolation and purification of a single LAV viral immunogen/antigen. The disclosure does **not** describe suitable immunization regimens that are capable of producing LAV-specific antibodies. Finally, the disclosure does *not* describe the isolation and purification of

LAV-specific antibodies. While it is noted that page 13 of the disclosure briefly mentions that the identified DNA sequences can be used "for achieving the expression of LAV viral antigens for diagnostic purposes as well as for the production of a vaccine against LAV", nevertheless, this vague recitation merely appears to be a wish to obtain reagents which were clearly never contemplated or in applicants' possession. Nothing in this passage would lead the skilled artisan to conclude that applicants' were in possession of the claimed invention.

Response to Arguments

Applicants response did not contain any new arguments pertaining to the written description rejection. Accordingly, as previously set forth, applicants asserted that the Examiner agrees that the claimed restriction fragments encode proteins and polypeptides. The Examiner does not concur with this assessment. As noted *supra*, the disclosure failed to provide any detailed nucleotide sequence data demonstrating that the cloned restriction fragments were in-frame and capable of coding a bona fide viral antigen/immunogen. The lentiviruses exist as a quasispecies and display considerable genotypic and phenotypic heterogeneity. Thus, in any given library, both replication-competent and replication-deficient forms will be present. Moreover, the reverse transcriptase employed in the preparation of cDNA libraries suffers from infidelity often introducing mutations into the strand or sequence being copied. Thus, simply identifying a restriction fragment from a novel virus does not prove conclusively that said fragment encodes a bona fide viral antigen/immunogen. The disclosure failed to perform a detailed molecular characterization of any of the fragments of interest. Thus, it simply is not know whether they encode full-length viral proteins, truncated forms thereof, unrelated proteins because of frame-shifting, or are entirely non-coding. The

disclosure simply does not address this issue.

Second, contrary to applicants' assertion, the specification does not provide literal support for the proteins or polypeptides encoded by the restriction fragments of interest. The passages relied upon merely state that restriction fragments "can be cloned into expression vectors" and "the resultant proteins purified." As noted in the preceding paragraph, there is no indication that the restriction fragments are capable of coding for any given LAV antigen or immunogen. The disclosure does **not** describe the detailed molecular characterization of these restriction fragments. Thus, it is simply **not known** if they correspond to bona fide LAV open reading frames. In fact, the applicants do **not** even know if suitable initiation codons are present in these sequences. The applicants do **not** know if these fragments are in the proper phase. Thus, it would be readily manifest to the skilled artisan that applicants never prepared suitable expression vectors, transfected suitable cell lines, and isolated and purified suitable viral antigens.

Third, applicants assert that the disclosure literally describes a "need" for LAV-specific antibodies. This argument clearly fails to support the appellants' position. Once again, a vague portion of the disclosure is relied upon that only discusses the possibility of using "antibodies" to identify the recombinantly produced antigens. This aspect of the argument does nothing to demonstrate that LAV-specific antigens/immunogens were prepared from the claimed restriction fragments. This point also fails to demonstrate that applicants isolated and prepared LAV-specific antibodies. The fact that the skilled artisan needs viral-specific immunological reagents to assess the immunoreactivity of any given antigen does not place the claimed invention in applicants' possession.

Fourth, contrary to applicants' arguments, the disclosure does

not provide literal support for the use of the claimed proteins and polypeptides. Applicants again rely upon a generic statement in the disclosure that simply states that the restriction fragments of the invention can be used for "achieving the expression of LAV viral antigens for diagnostic purposes" particularly as it applies to the core and envelope regions. Contrary to applicants' assertion, this passage does **not** describe the expression, isolation, and purification of a single LAV antigen from a single restriction fragment. This passage does **not** disclose a single diagnostic assay employing any given LAV antigen. There is no discussion of the specificity, reliability, or reproducibility of any given diagnostic assay employing LAV-specific antigens or antibodies. Once again, the skilled artisan would reasonably conclude that applicants were not in possession of the claimed invention at t he time of filing.

Finally, applicants argue that the use of the proteins and polypeptides as "immunogens" clearly illustrates that "raising antibodies" was clearly embodied in the disclosure. This argument is not tenable either upon perusal of the teachings of the specification. Once again, the passages relied upon fail to describe the isolation and purification of a single LAV immunogen, the immunization of suitable animals, the isolation and purification of resultant antibodies, and the characterization and analysis of said antibodies. This portion of the disclosure clearly fails to support the claimed invention. Thus, the skilled artisan upon perusal of the disclosure would reasonably conclude that applicants were not in possession of the claimed invention at the time of filing.

Finality of Office Action

Applicants are reminded that on the second or any subsequent examination or consideration by the examiner the rejection or other

action may be made final, 37 C.F.R. § 1.113. Since this is the second action following a rejection, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). **A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.**

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, James C. Housel, can be reached at (571) 272-0902. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related

Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

02 March, 2006